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Health and Environmental
Effects Profile for Mancozeb

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE
FOR MANCOZEB

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT The Health and Environmental Effects Profile for <u>Mancozeb</u> was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents. Quantitative estimates have been presented provided sufficient data are available. <u>Mancozeb</u> has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for <u>Mancozeb</u> is 2.9×10^{-2} mg/kg bw/day for oral exposure.		
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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEP's are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEP's will become part of the EPA RCRA docket.

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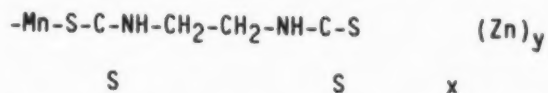
ADI	Acceptable daily intake
DNA	Deoxyribonucleic acid
LC ₅₀	Concentration lethal to 50% of recipients (and all other subscripted dosage levels)
LD ₅₀	Dosage lethal to 50% of recipients (and all other subscripted dosage levels)
TLC	Thin layer chromatography

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Mancozeb is the common name for [[1,2 ethanedylbis[carbamdithio-ato]](2-)] manganese, mixture with [[1,2 ethanedylbis[carbamdithio-ato]](2-)] zinc, formerly [ethylenebis[dithiocarbamate]] manganese mixture with [ethylenebis[dithiocarbamate]] zinc. Mancozeb was introduced as a fungicide under the trade name Dithane M-45 in 1961 by Rohm and Haas Co., British Crop Protection Council (BCPC, 1977). Other trade names include Vondozeb, Carmazine, Dithane S60, Dithane SPC, Dithane Ultra, F2966, Fore, Green-Daisen M, Karamate, Maneofol, Maneb-Zineb, Marzin, Nemispor, Policar MZ, Triziman, Zimanat and Zimman-Dithane (NIOSH, 1983).

Mancozeb is the coordination product of maneb and zinc, contains 20% manganese, 2.5% zinc and 77.5% ethylenebisdithiocarbamate and exists as a polymer in which zinc is firmly bound (Lyman, 1971). The structure of mancozeb is given below (Lyman, 1971; BCPC, 1977):



The Chemical Abstracts Service (CAS) Registry Number for mancozeb is 8018-01-7.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Mancozeb is a powder of grayish yellow color with the following physical properties (BCPC, 1977):

Melting Point:	Decomposes before melting
Flash Point:	137.8°C
Solubility:	Low solubility in water and most organic solvents
Stability:	Unstable at high temperature, in the presence of moisture or acid. It decomposes at a rate of 0.18%/month at 35°C under dry conditions.

1.3. PRODUCTION DATA

Mancozeb is produced in the United States by E.I. du Pont de Nemours and Co., Inc., LaPorte, TX, and by Rohm and Haas Co., Philadelphia, PA (SRI, 1983). Production data for the United States are unavailable. It is prepared by mixing an aqueous slurry of maneb and a soluble zinc salt and then drying the mixture (von Rumker et al., 1974).

1.4. USE DATA

It has been estimated that 10 million pounds of mancozeb were used in the United States in 1975 for the control of fungal diseases on a wide variety of fruits and vegetables (Ayers and Johnson, 1976).

2. ENVIRONMENTAL FATE AND TRANSPORT

Data regarding the fate and transport of mancozeb in soil are limited. In an abstract of a study, Lyman and Lacoste (1975) reported that mancozeb did not leach through sand when sprayed onto the surface of sand under field conditions, but was rapidly degraded microbially, with the evolution of CO_2 . Further details of the study were unavailable. In another abstract of a French study, Doneche and Seguin (1975) also indicated that soil microbes participated in the degradation of 10 mg mancozeb/kg soil in vitro, which was complete within 3 months. Again, further details were lacking. Blazquez (1973) sprayed mancozeb on the surface of prepared soil beds (Immokalee fine sand) at a rate of 2 pounds/100 gallons of water and found that ~36% disappeared in 1 day, and 65% in 6 days. None was detected on the thirteenth day from the date of spraying. No ethylenethiourea (ETU), a natural degradation product of ethylenebisdithiocarbamates (Sanborn et al., 1977), was found on any sampling day; no statement of the mechanism of mancozeb disappearance can be made. ETU, a carcinogen in animals (IARC, 1974, 1982), was degraded to ethyleneurea and CO_2 by both chemical and microbial means within 4 days in soil (Kaufman and Fletcher, 1973).

No other information regarding the fate or transport of mancozeb in soil was found. Since mancozeb is a coordination product having components of both maneb and zineb, it may be possible to draw some analogies to results obtained with these two fungicides. Nash and Beall (1980) conducted a closed microagroecosystem study and found that both maneb and zineb residues were detectable on the soil surface (Galestown sandy loam) after application for the duration of the 70-day observation. Neither compound, detected as ethylenediamine (EDA), penetrated below 1 cm soil depth, but both dissipated

with half-lives of 23 days for zineb and 36 days for maneb. The concentration of EDA in leachate water was only 0.45 $\mu\text{g/l}$ for zineb and 1.2 $\mu\text{g/l}$ for maneb.

Helling et al. (1974) compared the mobility of maneb and zineb in various soil types using soil TLC plates and 10 different species of fungi and 1 alga as bioassay systems for visualization. Zineb had an overall R_f of 0.01, while maneb had an overall R_f of 0.33 when Hagerstown silty clay loam was used. Likewise, zineb was virtually immobile on Lakeland sandy loam plates, Norfolk sandy loam, Barnes clay loam and Celeryville muck. Maneb was slightly more mobile than zineb. It is reasonable to assume that mancozeb will also have a low mobility in soil.

The fate of mancozeb in soil may depend upon its ability to volatilize. Nash and Beall (1980) reported that air concentrations of maneb and zineb in their closed microecosystem were $<20 \text{ ng/m}^3$. Both maneb and zineb have negligible vapor pressures (BCPC, 1977) so their low tendency to volatilize probably applies to mancozeb as well.

Information regarding the fate and transport of mancozeb in aquatic media is also limited. The main route of entry of mancozeb into water would probably be through suspended particles in runoff water, consistent with the experimentally observed tendency of the ethylenebisdithiocarbamates to sorb tightly to particulate matter. Lyman and Lacoste (1975) reported a half-life for mancozeb in water at pH 5-9 as <1 day. In a spray tank slurry of mancozeb (1 pound/100 gallons) 2.08 ppm ETU was formed after 1 minute and 3.62 ppm ETU was formed after 4 hours.

Blazquez (1973) reported residual concentrations of 100 ppm mancozeb in 1000 ml of deionized water maintained at 20°C to be 90% by day 1, 80% by day 7, 70% by day 14, and 60% by day 21. ETU was detected in the water on

day 7 in a ratio of 1 part ETU to 5 parts mancozeb. No residues were present on day 34. In ditches containing 500 g mancozeb/946 l water, 44% disappeared by day 1 and 80% by day 7. No ETU was present in the ditch water on the fourteenth day after application. These observations indicate that mancozeb is not only readily hydrolyzed in aquatic environments, but that other processes may degrade mancozeb in natural aquatic media.

No information regarding the photodegradation of mancozeb was located in the available literature; however, observations about the photodegradation of maneb and zineb may also apply to mancozeb. Iley and Fiskell (1963) noted that there was no difference in the rate of degradation of zineb exposed to sunlight or to darkness for as long as 19 months. Muskat and Schlemmer (1976) reported that when aqueous suspensions of maneb sprayed onto filter paper were exposed to ultraviolet light under moist conditions, all the maneb was converted to ETU within 15 days.

One degradation product of mancozeb is ETU, but ETU is readily photodegraded in aqueous media to ethylene urea, hydantoin and glycine sulfate (Cruickshank and Jarrow, 1973; Rhodes, 1977). In drainage ditch water, ETU was 90% degraded by sunlight in 24 days (Ross and Crosby, 1973).

Information regarding the fate and transport of mancozeb in air was not located. Both maneb and zineb have negligible vapor pressures (BCPC, 1977) and are therefore not likely to volatilize to a large extent. It is likely that this applies also to mancozeb. The major routes of entry of mancozeb into the atmosphere are more likely to be spray drift during application and drift in wind of mancozeb sorbed to soil particles. The extent of degradation in air will depend upon moisture content, temperature and photodegradation. The respective half-lives of maneb and zineb in air were determined to be 7-14 days and 11-14 days (Nash and Beall, 1980). Therefore, mancozeb may have a half-life of between 7 and 14 days.

3. EXPOSURE

No monitoring data for mancozeb were contained in STORET, and no other information regarding ambient levels of zineb in soil, water or air was located in the available literature.

Besides occupational exposure, human exposure to mancozeb occurs primarily through residues on food. Duggan et al. (1966) monitored food for pesticides using the "total diet" approach (all the food consumed over a 2 week period by an 18-year-old male). These investigators collected 82 foods from 18 markets in Boston, MA, Kansas City, MO and Los Angeles, CA, separated them into 12 classes, and combined them in a slurry. Of the 216 composites analyzed, 5 were found to contain dithiocarbamate residues ranging from 0.4-0.8 ppm calculated as equivalent zineb concentration. These foods were mainly grain and cereal products and raw and processed leafy vegetables.

Concern over exposure to mancozeb residues on food is enhanced by the increased levels of ETU found in cooked and processed foods. Little, if any, ETU was found on harvested apples, tomatoes, grapes, pears, potatoes, cucumbers, squash or cantaloupes; however, the acts of cooking, processing or storing such foods have resulted in detectably increased levels of ETU (Ross et al., 1978; Ripley and Cox, 1978; Ripley et al., 1978; Ripley and Simpson, 1977; Pease and Holt, 1977 and Watts et al., 1974).

4. PHARMACOKINETICS

Only one study regarding the pharmacokinetics of mancozeb was found in the available literature. Lyman (1971) administered ^{14}C -mancozeb (prepared from ^{14}C -ethylenediamine) in a dose of 100 mg/kg/day to 6 rats by gavage for 7 days. The rats were killed on the eighth day, and urine, feces and tissues were examined for radioactivity. Of the administered radioactivity, 70.9% was excreted in the feces, 15.5% in the urine, 3.98% was found in cage washings, 0.18% in intestinal washings, 0.31% in organ and tissue samples and 0.96% in the carcass. In the urine, 5.6% of the recovered radioactivity was represented by ethylenebisisothiocyanate sulfide, 28.0% by ethylenethiourea (ETU), 12% by ethylene urea, 19% by N-acetyl ethylenediamine, 1.0% by N-formyl ethylenediamine and 3.5% by ethylenediamine. In the feces, 47% of recovered radiolabel was represented by unchanged mancozeb, 7.5% by EBIS, 6.0% by ETU and 2.0% as ethylene urea. When expressed in terms of percentage of administered dose per gram of tissue weight, the distribution data indicated mancozeb (or a metabolite) accumulated in the thyroid of these animals, while levels in other tissue were relatively low.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent information regarding the carcinogenic potential of mancozeb was not found in the available literature, and this compound is not scheduled for testing by the National Toxicology Program (NTP, 1983).

5.2. MUTAGENICITY

Mancozeb has been tested for mutagenicity in bacterial, yeast, plant, insect, rodent and human systems (Waters et al., 1982; DeLorenzo et al., 1978; Njagi and Gopalan, 1981; Vasudev and Krishnamurthy, 1980; Newton and Lilly, 1979; Georgian et al., 1983). Negative responses were observed in reverse mutation assays in Salmonella typhimurium, Escherichia coli and the rec assay in Bacillus subtilis assay systems (Waters et al., 1982; De Lorenzo et al., 1978) and in a Drosophila melanogaster sex-linked recessive lethal assay (Vasudev and Krishnamurthy, 1980). Mancozeb gave positive responses for mitotic recombination in Saccharomyces cerevisiae (Waters et al., 1982); for increased frequency of chromosome aberrations in Vicia faba (Njagi and Gopalan, 1981), in rat lymphocytes in vivo (Newton and Lilly, 1979), in rat bone marrow cells in vivo, in human blood cells in vitro (Georgian et al., 1983) and for unscheduled DNA synthesis in human lung fibroblasts in vitro (Waters et al., 1982). Details of these studies are given in Table 5-1.

5.3. TERATOGENICITY

Only one study on the teratogenic effects of mancozeb was available. Larsson et al. (1976) administered mancozeb by gavage to pregnant NMRI mice and to pregnant Sprague-Dawley rats (day 0 of pregnancy was designated as the morning when vaginal plugs were present in mice or when vaginal smears contained spermatozoa in rats) on day 9 or 13 of gestation in mice and on

TABLE 5-1

Mutagenicity Testing of Mancozeb

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response*	Comment	Reference
Reverse mutation	<u>Salmonella typhimurium</u>	plate incorporation	6 concentrations up to 10 mg/plate	±S9	-	In strains TA1535, TA15737, TA1538, TA 100 and TA98	Waters et al., 1982
Reverse mutation	<u>S. typhimurium</u>	plate incorporation	NR	±S9	-	In strains TA1535, TA1537, TA1538, TA 100 and TA98	De Lorenzo et al., 1978
Reverse mutation	<u>Escherichia coli</u>	NR	6 concentrations up to 10 mg/plate	±S9	-	NC	Waters et al., 1982
Primary DNA damage	<u>E. coli</u>	spot test	NR	-S9	-	NC	Waters et al., 1982
Rec assay	<u>Bacillus subtilis</u>	spot test	NR	-S9	-	NC	Waters et al., 1982
Mitotic recombination	<u>Saccharomyces cerevisiae</u>	NR	NR	±S9	+	+ = >3-fold dose-related increase in absolute no. of recombinants/mg and in relative no of recombinants/10 ⁵ survivors	Waters et al., 1982
Chromosome aberrations	<u>Vicia faba</u>	roots submerged in solutions containing 10-10 ⁴ ppm	10-10 ⁴ ppm	NR	+	dose-related (range/NR) increase in frequency of aberrations	Njagi and Gopalan, 1981
Sex-linked recessive	<u>Drosophila melanogaster</u>	larval feeding	5, 10 or 15 mg/100 ml media	NR	-	NC	Vasudev and Krishnamurty, 1980
Chromosome aberrations	rat lymphocytes	in vivo, route NR	NR	NR	+	This was reported only as an abstract.	Newton and Lilly, 1979

TABLE 5-1 (con't)

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response*	Comment	Reference
DNA damage REP assay	<i>E. coli</i> po/A (p347F)	spot test	NR	±S9	-	NC	Waters et al., 1982
REM Rec assay	<i>B. subtilis</i> H45 (rec A)	spot test	NR	±S9	-	NC	Waters et al., 1982
DNA damage YEC enhanced mitotic recombination	<i>Saccharomyces cerevisiae</i> D3	NR	5 concentrations	±S9	-	Dose response: increase >3-fold in absolute number of mitotic recombination/na	Waters et al., 1982
Unscheduled DNA synthesis	human lung fibroblast	cell culture	5 concentrations	±S9	-	NC	Waters et al., 1982

*Responses: +, positive; -, negative; ±, negative with and without S9 activation system; ±, positive with and negative without S9 activation system

NC = No comment

NR = Not reported

day 11 of gestation in rats at doses of 0, 380, 730 or 1330 mg/kg. The animals were killed on day 18 of gestation. No treatment-related effects in mice were observed in the dams or fetuses.

The results in rats were as follows. No effects were seen at 380 mg/kg. An increased incidence of grossly malformed fetuses was observed only in the high-dose group (22/87 viable fetuses from 7 litters in this group were abnormal in contrast to 1/102 viable fetuses in the control group). Gross anomalies in the high-dose rat fetuses included cleft palate (16/87), brachygnathia (9/87), low external ears (9/87), open eye (4/87), exophthalmia (2/87), anophthalmia (5/87), exencephaly (1/87), hydrocephaly (20/87), meromelia (9/87), adactyly or oligodactyly (14/87), short tail (21/87), umbilical hernia (9/87), edema (9/87) and neck constriction (9/87). Of the 87 viable high-dose fetuses, 30 were examined for skeletal deformities and 14 were examined for other internal abnormalities. The incidences of these anomalies were: fused ribs, 1/30; malformed vertebral column, 7/30; malformed extremities, 1/30; hydrocephaly, 7/14; malformed spinal cord, 3/14; malformed eyes, 2/14; and internal hemorrhage, 1/14. For rats of the 730 mg/kg group, 0/61 viable fetuses had gross malformations, 9/61 viable fetuses had superficial hemorrhages and 1/10 fetuses examined for internal abnormalities had dilated renal pelvis. The 1 malformed control fetus had a short tail. None of the 36 control fetuses examined for skeletal abnormalities were found to have such abnormalities. The only internal malformation found in 14 control fetuses was an internal hemorrhage (in 1 fetus).

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of mancozeb were not located in the available literature.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Pertinent data regarding the chronic or subchronic toxicity of mancozeb were not located in the available literature.

5.6. OTHER RELEVANT INFORMATION

The oral LD₅₀ for mancozeb was reported as 14,000 mg/kg for male rats and 12,800 mg/kg for female rats (Ivanova-Chemishanska, 1969) or as 6750 mg/kg for rats (Georgian et al., 1983). NIOSH (1983) reported a value of 5000 mg/kg for the oral LD₅₀ in rats.

Mancozeb has been found to cause allergies and contact dermatitis in farm workers (Kleibl and Rackova, 1980; Peachey, 1981; Lee et al., 1981). Addition of mancozeb to the diet of rats caused decreased activities of microsomal p nitro-anisole O-demethylase and glutathione peroxidase, and increased the activity of microsomal glutathione-S-transferase (Puzynska, 1981).

6. AQUATIC TOXICITY

6.1. ACUTE

Mancozeb has been tested for acute toxicity and lethality in several species of fish (Table 6-1). A Japanese study (Baba et al., 1974) reported the yellow-tail, Seriola dorsalis, to be the most sensitive with a 24-hour LC_{50} of 0.23 mg/l. Trout were moderately sensitive to mancozeb with 48-hour LC_{50} values of 1.9 mg/l (Spehar et al., 1982) or 1.85 mg/l (Svobodova, 1980) for rainbow trout and 0.5 mg/l for the Japanese saghalin trout (Kuroda, 1975). The carp, Cyprinus carpio, was the most tolerant of mancozeb exposure, having a 48-hour LC_{50} of 24.0 mg/l (Spehar et al., 1982), and a 6-day exposure at 5.0 mg/l resulted in no toxic effects (Antychowicz et al., 1979). Studies with the harlequin fish, Rasbora heteromorpha, reported a 24-hour LC_{50} of 4.2 mg/l and a 48-hour LC_{50} of 4.0 mg mancozeb/l (Tooby et al., 1975; McKim et al., 1976). The guppy was slightly more resistant than the rainbow trout, having a 48-hour LC_{50} of 2.2 mg mancozeb/l (Spehar et al., 1982).

The growth of the ciliate, Tetrahymena pyriformis, was inhibited by 0.01, 0.1, 1.0, 10.0 and 100 mg/l mancozeb (Toth and Tomasovicova, 1979).

6.2. CHRONIC TOXICITY

Pertinent data regarding the chronic effects of mancozeb on aquatic organisms were not located in the available literature.

6.3. PLANT EFFECTS

Heckman (1981) reported on the effects of pesticides, including mancozeb, used in orchards on the aquatic and littoral plants in run-off streams and ditches. Comparing the occurrence of plant species in the streams during 1978-1980 with that reported during 1951-1957 before the use of herbicides, (Garms, 1961; Heckman, 1981) reported a few species that were

TABLE 6-1

Acute Lethal Effects of Mancozeb to Fish

Species	Duration	Concentration (mg/l)	Method	Effect	Reference
Rainbow trout <u>Salmo gairdneri</u>	48 hour	1.9	NR	LC50	Spehar et al., 1982
Rainbow trout <u>Salmo gairdneri</u>	48 hour	1.85	NR	LC50	Svobodova, 1980
Sagehen trout (fry)	48 hour	0.5	NR	lethal	Kuroda, 1975
Carp, <u>Cyprinus</u> <u>carpio</u>	6 day	5.0	NR	none	Antychowicz et al., 1979
Carp, <u>Cyprinus</u> <u>carpio</u>	48 hour	4.0	NR	LC50	Spehar et al., 1982
Harlequin fish <u>Rasbora</u> <u>heteromorpha</u>	48 hour	4.0	NR	LC50	McKim et al., 1976
Harlequin fish <u>Rasbora</u> <u>heteromorpha</u>	24 hour 24 hour 48 hour 48 hour	3.9 4.2 3.4 4.0	constant flow constant flow constant flow constant flow	LC10 LC50 LC10 LC50	Tooby et al., 1975 Tooby et al., 1975 Tooby et al., 1975 Tooby et al., 1975
Guppy, <u>Poecilia</u> <u>reticulata</u>	48 hour	2.2	NR	LC50	Spehar et al., 1982
Yellowtail, <u>Sciaenops</u> <u>dorsalis</u>	24 hour	0.23	NR	LC50	Raba et al., 1974

NR = Not reported

no longer present in the area or were decreased in numbers, but no effect from pesticides was implied.

No additional data regarding the effects of mancozeb on aquatic plants were located in the available literature.

6.4. RESIDUES

Belamie et al. (1977) reported that residues of dithiocarbamate fungicides used on cress fields were detected in fish in streams near the cress fields. The residues were concentrated in the liver and kidney of fish. Residues of the fungicides were also detected in river sediment of the area.

6.5. OTHER RELEVANT INFORMATION

Additional data relevant to the toxic effects of mancozeb on aquatic organisms were not located in the available literature.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

An abstract indicated that a review of research to ensure the safety of mancozeb exists, but the review was unavailable (De la Graviere et al., 1979). Also, an abstract of a Chinese study (Li et al., 1981) indicated that there are estimates of crop maximum permissible residues in Taiwan.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of mancozeb were not located in the available literature.

8. RISK ASSESSMENT

No information regarding the carcinogenicity of mancozeb was found in the available literature, and the lack of information regarding the chronic or subchronic toxicity of mancozeb precludes the calculation of an ADI value. Mancozeb was found to be teratogenic in rats at a dose of 1330 mg/kg, with mild fetal effects at 730 mg/kg and no effects at 380 mg/kg (Larsson et al., 1976), but a single teratogenic study is inadequate for the derivation of an ADI. Mancozeb was also found to produce chromosomal aberrations in eukaryotic systems but was not mutagenic in prokaryotic systems (Waters et al., 1982; De Lorenzo et al., 1978; Njagi and Gopalan, 1981; Vasudev and Krishnamurthy, 1980; Newton and Lilly, 1979; Georgian et al., 1983). There is sufficient evidence that ETU, a degradation product and metabolite of mancozeb, is carcinogenic in experimental animals (IARC, 1974, 1982; 42 FR 40618). Moreover, the Carcinogen Assessment Group (CAG) of the U.S. EPA conducted a risk assessment for ethylenebisdicarbamate (EBDC) on the basis that a contaminant and metabolite, ETU, was carcinogenic (U.S. EPA, 1979). In light of the fact that ETU is also a metabolite and environmental breakdown product of mancozeb, further evaluation of its potential carcinogenicity is desirable.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment, however, can be presented in this chapter.

The CBI Appendix to this document reviews other animal studies from which an ADI of 1.995 mg/day for a 70 kg man (0.0285 mg/kg/day) was derived. The ADI was based on a dietary NOEL of 50 ppm (~2.85 mg/kg/day based on data supplied by the investigator) in rats in a 90-week study and an uncertainty factor of 100. The LOAEL was 100 ppm in the 90-week study in rats (~6 mg/kg/day) and in a 2-year feeding study in dogs (~4 mg/kg/day), and was the threshold for goitrogenic effects.

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APPENDIX: LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
EPCASR
Chemical Industry Notes

Most of these searches were conducted in February, 1983; a few were conducted March-May, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 7 and 8th), and the following secondary sources were reviewed:

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